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Proposed Registration Decision PRD2016-34

Cyazofamid

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Overview

Proposed Registration Decision for Cyazofamid

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Technical Cyazofamid Fungicide (Registration Number 27983) and Cyazofamid 400 SC Fungicide (Registration Number 27984), containing the technical grade active ingredient cyazofamid, to control diseases caused by the oomycete *Pythium* on turfgrass.

Cyazofamid 400 SC Fungicide is currently registered for use on multiple crops to control diseases caused by the oomycete *Pythium*. The detailed review of Technical Cyazofamid Fungicide and Cyazofamid 400 SC Fungicide can be found in the Regulatory Note REG2006-05, *Cyazofamid*.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Technical Cyazofamid Fungicide and Cyazofamid 400 SC Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on cyazofamid, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on cyazofamid, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Cyazofamid?

Cyazofamid is the active ingredient in Cyazofamid 400 SC Fungicide. It provides control of diseases caused by the oomycete *Pythium* on turfgrass.

Health Considerations

Can Approved Uses of Cyazofamid Affect Human Health?

Cyazofamid 400 SC Fungicide is unlikely to affect your health when used according to label directions.

Potential exposure to cyazofamid may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, the technical grade active ingredient cyazofamid was of low acute toxicity by the oral, dermal and inhalation routes. It was minimally irritating to the eyes and slightly irritating to the skin. It did cause an allergic skin reaction; consequently, the hazard signal words "POTENTIAL SKIN SENSITIZER" are required on the label.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

The acute toxicity of the end-use product Cyazofamid 400 SC Fungicide containing cyazofamid was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes, non-irritating to the skin and did not cause an allergic skin reaction.

Short-term and long-term (lifetime) animal toxicity tests were assessed for the potential for cyazofamid to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment included effects on the skin, heart and eyes. There was an indication that the young animal was more sensitive than the adult animal. The risk assessment is protective of the above-noted effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in test animals.

Residues in Water and Food

Dietary risks from food and drinking water are not of health concern.

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and children 1-2 years old, the subpopulation which would ingest the most cyazofamid relative to body weight, are expected to be exposed to less than 5% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from cyazofamid is not of health concern for all population subgroups.

Animal studies revealed no acute health effects relevant to a single dietary exposure event. Consequently, a single dose of cyazofamid is not likely to cause acute health effects in the general population (including infants and children).

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

No food residue data are required to support the registration of cyazofamid for use in/on turfgrass on golf courses and sod farms in Canada. For the MRLs for this active ingredient on various crop commodities, please refer to the Maximum Residue Limit Database in the Pesticides and Pest Management section of Health Canada's website.

Occupational Risks From Handling Cyazofamid 400 SC Fungicide

Occupational risks are not of health concern when Cyazofamid 400 SC Fungicide is used according to the label directions, which include protective measures.

Workers who mix, load or apply Cyazofamid 400 SC Fungicide, as well as field workers re-entering freshly treated golf courses and sod farms, can come into direct contact with cyazofamid residues on the skin. Therefore, the label specifies that anyone mixing/loading Cyazofamid 400 SC Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves and goggles, and that anyone applying Cyazofamid 400 SC Fungicide must wear a long-sleeved shirt and long pants. If the application is made with handheld equipment (backpack sprayer and turf gun) the

workers must also wear chemical-resistant gloves. The label also requires that workers do not enter treated areas in sod farms for 12 hours after application, and that workers and the general public do not enter treated areas in golf courses "until sprays have dried". Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the health risks to these individuals are not of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Risks in Residential and Other Non-Occupational Environments

Residential and non-occupational risks are not of health concern when Cyazofamid 400 SC Fungicide is used according to the label directions.

Adults, youth and children may be exposed to cyazofamid while golfing on courses treated with Cyazofamid 400 SC Fungicide. Based on the expected short- to intermediate-term duration of this activity, the health risk to children, youth and adults is not a concern. There are no residential turf uses of Cyazofamid 400 SC Fungicide.

Environmental Considerations

What Happens When Cyazofamid Is Introduced Into the Environment?

When used according to label directions, cyazofamid does not pose a risk of concern to the environment.

When cyazofamid is sprayed onto turfgrass to control plant diseases, it is broken down at a somewhat slow rate in soil. After spraying, cyazofamid will not move downward into the soil. Cyazofamid will not volatilize from the soil surface or from the turfgrass. It will not accumulate in plants and animals.

Cyazofamid will not affect earthworms, honeybees or most beneficial insects when it is used according to label directions. Also, there would be no harm to birds if they feed on vegetation and insects that might get contaminated with cyazofamid as a result of spraying. There is a small potential for harm to certain beneficial insects and small mammals if they feed on turf that is sprayed with cyazofamid. Plants adjacent to the area where cyazofamid is sprayed may also be affected.

Because cyazofamid may enter either freshwater or marine bodies of water, some organisms such as amphibians, marine invertebrates and algae can be affected by this pesticide. Therefore, appropriate precautionary label statements (for example, buffer zones) will be required. Cyazofamid will not affect freshwater or marine fish, freshwater invertebrates or aquatic plants as long as it is not sprayed directly onto water.

Value Considerations

What Is the Value of Cyazofamid 400 SC Fungicide?

Cyazofamid 400 SC Fungicide provides a new mode of action for resistance management of turf diseases caused by *Pythium* spp.

A high level of disease control is expected by turfgrass managers on golf courses and sod farms. Use of fungicides such as Cyazofamid 400 SC Fungicide maintains putting surfaces and the aesthetic quality of golf courses, sod and landscapes. It also minimizes costs associated with renovation or re-seeding of turf.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Cyazofamid 400 SC Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

As there is a concern with users coming into direct contact with cyazofamid on the skin or through inhalation of spray mists, anyone mixing/loading Cyazofamid 400 SC Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves and goggles. Anyone applying Cyazofamid 400 SC Fungicide must wear a long-sleeved shirt and long pants. If the application is made with handheld equipment (for example, backpack sprayer and turf gun) workers must also wear chemical-resistant gloves.

The Cyazofamid 400 SC Fungicide label requires that workers not enter treated areas in sod farms for 12 hours after application, and that workers and the general public not enter treated areas in golf courses "until sprays have dried". In addition, standard label statements to protect against drift during application are present on the label.

Environment

A hazard to small wild mammals and certain beneficial insects is indicated on the label.

Statements and no-spray buffer zones also appear on the label to reduce the risk of spray drift to aquatic and terrestrial habitats

Next Steps

Before making a final registration decision on cyazofamid, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on cyazofamid (based on the Science Evaluation section of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Cyazofamid

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Please refer to Regulatory Note REG2006-05: *Cyazofamid*.

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Please refer to Regulatory Note REG2006-05: *Cyazofamid*.

1.3 Directions for Use

Cyazofamid 400 SC Fungicide is to be applied at rates of 14.3 – 26.6 ml/100 m^2 (5.7 – 10.6 g a.i./100 m^2) on 14 – 21 day intervals. The recommended spray volume is 7.5 – 15.0 L of water/100m^2. Use the lower rate for the shortest interval and higher rate for the longest interval. When disease pressure is severe use the high rate and the short interval. After one application, alternate Cyazofamid 400SC Fungicide with at least one application of a fungicide having a different mode of action. The product may be applied up to three times per season with a maximum seasonal application rate of 80 ml/100 m^2 (32 g a.i./100m^2).

1.4 Mode of Action

Cyazofamid is a Fungicide Resistance Action Committee (FRAC) Group 21 fungicide that inhibits respiration of oomycete fungi. Cyazofamid prevents germination and formation of zoosporangia and growth of mycelia by inhibiting energy production within the fungal cells.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

Please refer to Regulatory Note REG2006-05, *Cyazofamid*.

2.2 Method for Formulation Analysis

Please refer to Regulatory Note REG2006-05, *Cyazofamid*.

2.3 Methods for Residue Analysis

Please refer to Regulatory Note REG2006-05, *Cyazofamid* and the Evaluation Report for Sub. No. 2008-1718 for residue analytical methods for data generation and enforcement purposes.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for cyazofamid was conducted previously and is summarized in the Regulatory Note REG2006-05, *Cyazofamid*. No new toxicology data were submitted for the current submission. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to cyazofamid.

Cyazofamid technical was of low acute toxicity via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes, slightly irritating to the skin and a potential dermal sensitizer. A metabolite of cyazofamid, CCIM, was highly acutely toxic by the oral route and of low acute toxicity by the dermal route. Other metabolites, CCIM-AM and DMSA, were considered to be of low acute toxicity by the oral route, and the environmental metabolite CTCA was slightly acutely toxic by the oral route. The EP, Cyazofamid 400 SC Fungicide, was of low acute toxicity via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes, non-irritating to the skin and was not a dermal sensitizer.

Absorption and excretion of cyazofamid was rapid. There was evidence of saturation as a minimum of 53% of the single low dose was absorbed, while absorption of a single high dose reached a maximum of 6% of the administered dose. Following repeated administration, less cyazofamid was absorbed and there was no evidence of accumulation in tissues/organs. Concentrations retained in tissues were very low, with the highest levels in the liver, kidneys, blood, muscle and fat.

The majority of studies in the toxicological database showed a lack of adverse effects up to and including the limit dose of testing. Exceptions were the long-term mouse and rat studies, which tested to levels approaching the limit dose, and the rat developmental toxicity study. In the 78-week mouse study at the high-dose in males, the only adverse finding was an increase in skin sores in high-dose males. In the 2-year rat study, adverse findings were limited to an increase in myocarditis and cataracts in the high-dose females. In the rat developmental toxicity study, an increase in wavy ribs in the fetuses in the absence of maternal toxicity occurred at the limit dose only.

Due to the timing of the original PMRA evaluation of cyazofamid, Regulatory Note REG2006-05, *Cyazofamid* did not address the *Pest Control Products Act* factor (PCPA factor) as required under the updated *Pest Control Products Act*. Consequently, the current document has included this consideration. The toxicology endpoints for use in human health risk assessment are presented in Table 1 in Appendix I.

Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA, including adverse effects to Canadian health or the environment. As of 6 May 2016, no human, domestic animal or environment incident reports involving cyazofamid had been submitted to the PMRA.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the Pest Control Products Act requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to infants and children, the standard complement of required studies was available, including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, there were no adverse findings in the two-generation reproductive toxicity study or the rabbit developmental toxicity study at doses up to and exceeding the limit dose of testing. In the rat developmental toxicity study, there was a slight increase in the incidence of a fetal skeletal variation, wavy ribs, observed at the limit dose of testing. These findings occurred in the absence of maternal toxicity.

Overall, the database is adequate for determining the sensitivity of the young and effects on the young are well characterized. Although the skeletal variations observed in the rat developmental toxicity study occurred at a non-maternally toxic dose, these findings were not considered serious in nature. For this reason, the PCPA factor was reduced to 3-fold when using the rat developmental toxicity study to establish the point of departure for assessing risk to women of child-bearing age. For exposure scenarios for children, the risk was considered well-characterized and the PCPA factor was reduced to 1-fold.

3.2 Acute Reference Dose (ARfD)

An acute reference dose was not required as there were no effects attributable to a single dose of cyazofamid.

3.3 Acceptable Daily Intake (ADI)

To estimate risk of repeat dietary exposure, the rat developmental toxicity study with a NOAEL of 100 mg/kg bw/day was selected for risk assessment. At the LOAEL of 1000 mg/kg bw/day, wavy ribs were observed in the fetuses. This study provides the lowest NOAEL in the database. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was reduced to 3-fold. Thus, **the composite assessment factor (CAF) is 300.**

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{100 \text{ mg/kg bw/day}}{300} = 0.33 \text{ mg/kg bw/day of cyazofamid}$$

Cancer Assessment

There was no evidence of carcinogenicity. Therefore, a cancer risk assessment is not necessary.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

For short-term and intermediate-term occupational exposures via the dermal and inhalation routes, the NOAEL of 100 mg/kg bw/day for fetal variations (wavy ribs) from the rat developmental toxicity study was selected for use in risk assessment. Wavy ribs occurred at the LOAEL of 1000 mg/kg bw/day.

The target Margin of Exposure (MOE) is 300, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The concerns outlined in the *Pest Control Products Act* Hazard Characterization section regarding the developmental toxicity endpoint are relevant to female workers of child-bearing age. For these reasons, an additional factor of 3-fold was applied to this endpoint.

Occupational exposure to cyazofamid is characterized as short- to intermediate-term in duration, and is predominantly by the dermal and inhalation routes. Exposure to cyazofamid when golfing on treated turf is characterized as short- to intermediate-term in duration, and is predominantly by the dermal route.

3.4.1.1 Dermal Absorption

Chemical-specific dermal absorption data were not submitted for cyazofamid. A dermal absorption estimate of 50% was supported for cyazofamid, using a weight-of-evidence approach from the physical/chemical properties of the active ingredient and dermal toxicity studies. This dermal absorption value was used in the risk assessments.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to cyazofamid during mixing, loading and application. Exposure to workers mixing, loading and applying Cyazofamid 400 SC Fungicide is expected to be short to intermediate term in duration and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for mixers/loaders/applicators applying Cyazofamid 400 SC Fungicide at the maximum rate in golf courses and sod farms using groundboom, backpack sprayer or turf gun.

The exposure estimates are based on mixers/loaders/applicators with the following personal protective equipment (PPE):

- a long-sleeved shirt and long pants, chemical-resistant gloves and goggles for all mixing/loading scenarios,
- a long-sleeved shirt and long pants for all application scenarios, and chemical-resistant gloves for backpack sprayer and turf gun.

As chemical-specific data for assessing human exposures were not submitted, dermal and inhalation exposures were estimated using the Pesticide Handlers Exposure Database (PHED), version 1.1 for workers involved in application using groundboom and backpack sprayers. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. Dermal and inhalation exposures for workers involved with low pressure handgun application were estimated using a study from the Outdoor Residential Exposure Task Force (ORETF).

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption value (50%). Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight. The dermal and inhalation exposure estimates were combined since they are both compared to the same toxicological endpoint of concern.

Exposure estimates were compared to the toxicological endpoint (no observed adverse effects level [NOAEL] of 100 mg/kg bw/day) to obtain the margin of exposure (MOE); the target MOE is 300. Table 3.4.2.1.1 presents the PHED and ORETF unit exposure values used. Table 3.4.2.1.2 presents the estimates of exposure and risk for Cyazofamid 400 SC Fungicide. Calculated MOEs are above the target MOE of 300 for workers who wear the personal protective equipment stated on the product label, and are, therefore, not of concern.

Table 3.4.2.1.1 PHED and ORETF unit exposure estimates for mixer/loader/applicators while handling Cyazofamid 400 SC Fungicide.

Exposure scenario		Unit Exposures (µg/kg a.i. handled)		
		Dermal	Inhalation[1]	Combined[2]
Single layer and CR gloves				
A	Liquid, open mix/load	51.14	1.6	27.17
B	Open cab groundboom application (single layer only; no gloves)	32.98	0.96	17.45
A+B	MLA Liquid, open ML + groundboom A (no gloves during A)	84.12	2.56	44.62
C	MLA Liquid - backpack	5445.85	62.1	2785.03
D	MLA Liquid - turf gun	785	4.0	396.50

CR = chemical-resistant, ML = mix/load, A = application, MLA = mixer/loader/applicator

[1] Moderate inhalation rate for backpack; light inhalation rate for all other scenarios.

All unit exposure values are from PHED, except for turf gun, which is from ORETF.

[2] Combined PHED or ORETF unit exposure =

(Dermal unit exposure × 50% dermal absorption) + (Inhalation unit exposure × 100% inhalation absorption)

Table 3.4.2.1.2 Chemical handler assessment for Cyazofamid 400 SC Fungicide

Exposure scenario		Combined Unit Exposure (µg/kg a.i. handled)[1]	Rate[2]	ATPD[3]	Exposure (mg/kg bw/day)[4]	Calculated MOE[5]
PPE: Single layer and CR gloves (gloves not required for groundboom application)						
A+B	MLA - Open ML + groundboom A	44.62	1.06 kg a.i./ha	30 ha/day {sod farm}	0.0177	5600
C	MLA - backpack	2785.03	0.00142 kg a.i./L	150 L/day	0.0074	13500
D	MLA - turf gun	396.50	1.06 kg a.i./ha	2 ha/day	0.0105	9500

CR = chemical-resistant, ML = mix/load, A = application, MLA = mixer/loader/applicator
[1] PHED or ORETF unit exposures from Table 3.4.2.1.1
[2] For backpack sprayer, the maximum application rate was calculated as 26.6 mL product/100 m^2 (10.64 g a.i./100 m^2) to be applied in 7.5 L of water per 100 m^2, equivalent to 0.00142 kg a.i./L
[3] Default Area Treated per Day (ATPD) values
[4] Daily exposure = (Total unit exposure × Area or Volume Treated per day × Rate) / (80 kg bw × 1000 µg/mg)
[5] Based on NOAEL = 100 mg/kg bw/day, target MOE = 300

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering golf courses and sod farms treated with Cyazofamid 400 SC Fungicide when conducting various activities. The duration of exposure is considered to be short-term for all re-entry activities. The primary route of exposure for workers re-entering treated areas would be through the dermal route. Inhalation exposure is not considered to be a significant route of exposure for people entering treated areas compared to the dermal route, since cyazofamid is relatively non-volatile (1.33×10^{-5} Pa) and as such, an inhalation risk assessment was not required.

Postapplication risk assessments were conducted with the maximum rate of Cyazofamid 400 SC Fungicide. Dermal exposure to workers entering treated areas was estimated by coupling transferable turf residue (TTR) values with activity-specific transfer coefficients and an exposure duration of 8 hours per day.

Chemical-specific TTR data were submitted. The TTR study was designed to determine transferable residues of cyazofamid from turf treated with a soluble concentrate formulation containing 34.5% of cyazofamid at a target of 1.12 kg a.i./ha. The product was applied three times, seven days apart. The study was conducted in one location in North Carolina, where the product was applied using a tractor-mounted platform boom sprayer. Transferable residues were sampled using the modified California roller method for TTR. Triplicate TTR samples were collected prior to the first application (pre-treatment), 0, 1, 2, 3, 5 and 6 days after the first application, 0, 1, 2, 3, 5 and 6 days after the second application, and 0, 1, 2, 3, 5, 7, 10 and 14 days after the last application (DALA). The TTR study was considered acceptable for risk assessment purposes. The application method and use pattern of the study is relevant to the Canadian use of cyazofamid on turfgrass. The peak TTR value for total cyazofamid residues from the study (0.7% of the application rate) was used in the postapplication risk assessment for Cyazofamid 400 SC Fungicide.

For postapplication risk, the dermal exposure estimates were compared to the toxicological endpoint (NOAEL = 100 mg/kg bw/day) to obtain the MOE; the target MOE is 300. Table 3.4.2.2.1 presents the calculated MOEs on the day of application and the resulting restricted entry intervals (REIs), which are not of concern.

Table 3.4.2.2.1 Postapplication exposure and risk estimates on the day of application for golf courses and sod farms treated with Cyazofamid 400 SC Fungicide

Re-entry activity	Peak TTR ($\mu g/cm^2$)[a]	Transfer Coefficient (cm^2/hr)[b]	Dermal Exposure (mg/kg bw/day)[c]	MOE[d]	REI
Golf course – Transplanting/ Planting; **Sod farm** – Slab harvesting, Transplanting/Planting	0.0777	6700	0.0260	3800	**Golf course** – Until sprays have dried; **Sod farm** – 12 hours

[a] Peak TTR value from submitted study, observed one hour after the last application
[b] Transfer coefficients from the Agricultural Reentry Task Force (ARTF)
[c] Dermal Exposure = (Peak TTR × Transfer Coefficient × 8 hours/day × 50% DAF)/(80 kg bw × 1000 µg/mg)
[d] Based on NOAEL= 100 mg/kg bw/day, target MOE = 300

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

Cyazofamid 400 SC Fungicide is not a domestic product; therefore, a residential handler assessment was not required.

3.4.3.2 Postapplication Exposure and Risk

Since Cyazofamid 400 SC Fungicide is for use on turfgrass in golf courses, there is potential for recreational postapplication exposure to the general population entering treated areas. The duration of exposure for golfing is considered to be short-term. The primary route of exposure for these individuals would be through the dermal route. Cyazofamid is considered non-volatile and it is not an inhalation concern for postapplication exposure.

Exposure was assessed according to equations and parameters stated in the 2012 United States Environmental Protection Agency Residential Standard Operating Procedures. Dermal exposure from golfing was assessed for adults (16 years plus), youth (11-<16 years) and children (6-<11 years). Chemical-specific TTR values were used to assess postapplication exposure on the day of application (0.7% of the application rate).

Dermal postapplication risk was calculated using the dermal absorption value (50%) and the toxicological endpoint for short- to intermediate-term dermal exposure (NOAEL = 100 mg/kg bw/day). Table 3.4.3.2.1 presents the calculated MOEs on the day of application for recreational dermal exposure; which are above the target MOE of 300, and therefore, not of concern.

Table 3.4.3.2.1 Dermal recreational postapplication exposure and risk from the use of Cyazofamid 400 SC Fungicide on the day of last application

Re-entry activity	Rate (kg a.i./ha)	# Appls (min RTI)	Peak TTR[1] (µg/cm²)	Age (yrs)	TC[2] (cm²/hr)	ED[3] (hr/day)	BW[4] (kg)	Exposure[5] (mg/kg bw/day)	MOE[6]
Golfing	1.06	3 appl (14 days)	0.0777	16+	5300	4	80	0.0103	9700
				11-<16	4400	4	57	0.0120	8300
				6-<11	2900	4	32	0.0141	7100

[1] Peak TTR value from submitted study, observed one hour after the last application
[2] TC = Transfer coefficients from ARTF
[3] ED = exposure duration
[4] BW = body weight
[5] Exposure = (Peak TTR × TC × ED × 50% DAF)/(BW × 1000 µg/mg)
[6] Based on NOAEL= 100 mg/kg bw/day, target MOE = 300

3.4.3.3 Aggregate Exposure

Cyazofamid is used on food crops and on golf courses. Since toxicological endpoints for short- to intermediate-term dermal exposure and chronic dietary exposure are the same, dermal exposure can be aggregated with chronic dietary (food plus drinking water) exposure.

Aggregate risk was calculated using the NOAEL of 100 mg/kg bw/day. Table 3.4.3.3.1 presents the aggregate MOEs on the day of application, which are above the target MOE of 300 and, therefore, not of concern.

Table 3.4.3.3.1 Aggregate risk from the use of Cyazofamid 400 SC Fungicide

Age group	Exposure (mg/kg bw/day)		Aggregate MOE[3]
	Dermal[1] (Golfing)	Chronic Dietary (Food + Drinking Water)[2]	
Adults (16+)	0.0103	0.0070	5700
Youth (11-16)	0.0120	0.0058	5600
Children (6-11)	0.0141	0.0088	4300

[1] Dermal exposure from Table 3.4.3.2.1
[2] Chronic dietary (food + drinking water) exposure were derived from the DEEM-FCID software
[3] Aggregate MOE = NOAEL / (Dermal exposure + Chronic dietary exposures)
MOEs are based on NOAEL = 100 mg/kg bw/day, target MOE = 300 for both dermal and oral exposure

3.4.3.4 Bystander Exposure and Risk

For Cyazofamid 400 SC Fungicide applied to turf in golf courses, the risk to bystanders is considered negligible as exposure to spray drift is not expected to exceed the exposure for mixers/loaders and applicators.

3.5 Food Residues Exposure Assessment

3.5.1 Concentrations in Drinking Water

3.5.1.1. Application Information and Model Inputs

Cyazofamid is a fungicide proposed for expansion for use to turf at an application rate of 3 applications of 1060 g a.i./ha, at 14 day intervals, for a total yearly application of 3180 g a.i./ha. Application information and the main environmental fate characteristics used in the models are summarized in Table 3.5.1.1.1.

Table 3.5.1.1.1 Major groundwater and surface water model inputs for Level 1 assessment of cyazofamid

Type of Input	Parameter	Value
Application Information	Crop(s) to be treated	Turf
	Maximum allowable application rate per year (g a.i./ha)	3180
	Maximum rate each application (g a.i./ha)	1060
	Maximum number of applications per year	3
	Minimum interval between applications (days)	14
	Method of application	Ground spray
Environmental Fate Characteristics of combined residues (cyazofamid, CCIM, CCIM-AM and CTCA)	Hydrolysis half-life at pH 7 (days)	Stable
	Photolysis half-life in water (days)	29.5d
	Adsorption K_{OC} (mL/g)	488 (20^{th} percentile of 4 K_{OC} values for CCIM)
	Aerobic soil biotransformation half-life (days)	53 (80^{th} percentile of four values)
	Aerobic aquatic biotransformation half-life (days)	112 (higher of two values)
	Anaerobic aquatic biotransformation half-life (days)	255 (only value available)
Cyazofamid	Hydrolysis half-life at pH 7 (days)	12.2
	Photolysis half-life in water (days)	0.024
	Adsorption K_{OC} (mL/g)	1333 (20^{th} percentile of 4 K_{OC} values for cyazofamid)
	Aerobic soil biotransformation half-life (days)	9.32 (80^{th} percentile of four values)
	Aerobic aquatic biotransformation half-life (days)	16.6 (higher of two values)
	Anaerobic aquatic biotransformation half-life (days)	13 (only value available)

3.5.1.2 Estimated Concentrations in Drinking Water Sources: Level 1 Modelling

Estimated environmental concentrations (EECs) of cyazofamid combined residues, (cyazofamid, CCIM, CCIM-AM and CTCA) in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of cyazofamid combined residues in groundwater were calculated using the SWCC model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PRZM-GW are average concentrations in the top 1 metre of the water table. EECs of cyazofamid combined residues in surface water were calculated using SWCC, which simulates pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in a vulnerable drinking water source, a small reservoir.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EEC estimate is expected to allow for future use expansion into other crops at this application rate. Table 3.5.1.1.1 lists the application information and main environmental fate characteristics used in the simulations. Twenty six initial application dates between April and October were modelled. The model was run to simulate a 50-year period for all scenarios. The largest EECs of all selected runs are reported in Table 3.5.1.2.1 below.

Table 3.5.1.2.1 Level 1 Estimated Environmental Concentrations of Cyazofamid Residues in Potential Drinking Water Sources

Compound	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)	
			Reservoir	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
Cyazofamid+CCIM+CCIM-AM+CTCA	1.2	1.2	117	22

Notes:
[1] 90th percentile of daily average concentrations
[2] 90th percentile of 365 day moving average concentrations
[3] 90th percentile of the peak concentrations from each year
[4] 90th percentile of yearly average concentrations

Details of water modelling inputs and calculations are available upon request.

3.5.2 Residues in Plant and Animal Foodstuffs

Please refer to the Regulatory Note REG2006-05 and the Evaluation Report for Sub. No. 2008-1718 for previously reviewed data. The information captured herein only relates to the changes in dietary exposure due to the modification in the drinking water assessments to support the registration of cyazofamid for use on turf in Canada.

3.5.3 Dietary Risk Assessment

A chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™).

3.5.3.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the basic chronic analysis for cyazofamid: 100% crop treated, default processing factors, residues of crop and animal commodities based on Canadian MRLs and American tolerances for imported commodities. The basic chronic dietary exposure from all supported cyazofamid food uses (alone) for the total population, including infants and children, and all representative population subgroups, is less than 5% of the acceptable daily intake (ADI). Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that the chronic dietary exposure to cyazofamid from food and drinking water is 2.3% (0.007515 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1-2 years old at 4.9% (0.016188 mg/kg bw/day) of the ADI.

3.5.3.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified.

3.5.4 Aggregate Exposure and Risk

Given that turfgrass in golf courses can be treated with Cyazofamid 400 SC Fungicide, there is potential for exposure to cyazofamid through the diet, as well as activities related to golf. An aggregate risk assessment for cyazofamid was conducted to include the dietary exposure from food and drinking water sources and the dermal exposure from the use on golf courses. The aggregate exposure for golfers, including the sum of the chronic dietary exposure and the dermal exposure incurred at the golf course for children, youth and adults, are not of health concern.

3.5.5 Maximum Residue Limits

Please refer to the Maximum Residue Limit Database in the Pesticides and Pest Management section of Health Canada's website for the established MRLs for cyazofamid.

The nature of the residues in animal and plant matrices, analytical methodology and residue trial data were assessed under Regulatory Note REG2006-05 and the Evaluation Report for Sub. No. 2008-1718. The chronic dietary risk estimates are summarized in Table 11 in Appendix I.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Please refer to Regulatory Note REG2006-05, *Cyazofamid*.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse ecological effects. This integration is achieved by comparing exposure concentrations (in other words., the expected environmental concentration (EEC)) with concentrations at which adverse effects occur (for example, toxicity endpoints such as LC_{50}, LD_{50}, NOEC or NOEL). For characterizing acute risk, acute toxicity

values (for example, LC_{50}, LD_{50}, and EC_{50}) are divided by an uncertainty factor. The uncertainty factor is used to account for differences in inter- and intra-species sensitivity as well as varying protection goals (for example, community, population, individual). Thus, the magnitude of the uncertainty factor depends on the group of organisms that are being evaluated (for example, 10 for fish, 2 for aquatic invertebrates). The difference in value of the uncertainty factors reflects, in part, the ability of certain organisms at a certain trophic level (that is, feeding position in a food chain) to withstand, or recover from, a stressor at the level of the population. When assessing chronic risk, the NOEC or NOEL is used and an uncertainty factor is not applied.

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the RQ is then compared to the level of concern (LOC = 1 for most species, 0.4 for pollinators and 2 for beneficial arthropods (acute screening tests for predatory mite and parasitoid wasp)). If the screening level RQ is below the LOC, the risk is considered negligible and no further risk characterization is necessary. If the screening level RQ is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

The environmental risk of cyazofamid and its related end-use product, Cyazofamid 400 SC Fungicide, to non-target organisms was assessed based upon the maximum annual application rate of 3180 g a.i./ha to turf (3 × 1060 g a.i./ha, with a 14-day application interval). Ecotoxicity endpoints used to assess risk from turf use were obtained from the Regulatory Note REG2006-05, *Cyazofamid*.

The expected environmental concentrations (EEC) of cyazofamid in soil, water and food sources for birds and small wild mammals are summarized in Table 2 through Table 7 in Appendix I.

4.2.1 Risks to Terrestrial Organisms

Table 8 of Appendix I summarizes the risk to terrestrial organisms.

To assess the potential for adverse effects, screening level EECs in the terrestrial environment were calculated based on a direct application of 3 x 1060 g a.i./ha at a 14-day interval. For the EEC in soil, an aerobic soil DT_{50} of 53 days was considered, thereby resulting in a cumulative application rate in soil of 2677.7 g a.i./ha and a corresponding EEC in soil of 1.2 mg a.i./kg soil. For EEC on plant surfaces, a half-life of 10 days was considered, resulting in a cumulative application rate on foliage of 1614 g a.i./ha.

Earthworms

Based on the reported no-observable effect concentration (NOEC), the risk quotient (RQ) for earthworms was 0.0012. Thus, the risk of lethal and sub-lethal effects to earthworms is negligible for the application of cyazofamid to turf at the maximum proposed annual rate.

Honeybees

Cyazofamid was classified as relatively non-toxic to honeybees according to the classification by Atkins *et al.* (1981) based on the reported toxicity for oral and contact exposures. An RQ was also determined based on conversion of the NOEC to an application rate of 112.0 kg a.i./ha. The RQ was therefore 0.03 (3.18 kg a.i./ha ÷ 112 kg a.i./ha) indicating that cyazofamid applied to turf at the maximum annual rate poses negligible risk to bees.

Other arthropod species:

The risk of cyazofamid to beneficial arthropods was assessed using the parasitic wasp (*Aphidius rhopalosiphi*). On the basis of reduction in beneficial capacity of wasps, the RQ was 16.0, indicating that cyazofamid may pose a risk to beneficial arthropods.

Birds

Wild upland game birds and waterfowl, as represented by bobwhite quail and mallard ducks, respectively, could be exposed to cyazofamid residues by consuming treated vegetation or contaminated prey.

For the risk based on acute oral toxicity, it would take a bobwhite quail at least 82.6 days of continuous consumption of a cyazofamid-contaminated diet to attain a dose equivalent to that administered in the laboratory by gavage that had no-observable effect on the laboratory population. Note that feeding on contaminated food sources for less than one day to reach the endpoint of concern is considered a potential risk. Therefore, cyazofamid poses a negligible risk to bobwhite quail when applied at the maximum rate to turf.

For the risk based on dietary exposure and reproductive effects in the bobwhite quail and mallard duck, the resulting RQs were 0.01-0.06. Cyazofamid therefore poses a negligible risk to bobwhite quail and mallard ducks when applied at the maximum rate to turf.

Small mammals

Small wild mammals such as rats, mice, and rabbits may be exposed to residues of cyazofamid by consuming of sprayed vegetation and contaminated prey.

The risk to small wild mammals from acute exposure to cyazofamid is expected to be negligible.

A rat would require 35.8 days of continuous feeding on cyazofamid-contaminated food sources to reach a dose equivalent to that administered in the laboratory by gavage that killed 50% of the test population (LD_{50} > 5000 mg a.i./kg bw). Similarly for the mouse, 34 days of continuous feeding on cyazofamid-contaminated food sources is needed to reach a dose equivalent to that administered in the laboratory by gavage that killed 50% of the test population (LD_{50} > 5000 mg a.i./kg bw). In addition, based on the gavage study and a NOAEL of 1000 mg/kg bw/d developmental effects in rabbit would require 27.4 days of continuous feeding on cyazofamid-contaminated food sources. Therefore, cyazofamid poses a negligible risk to small wild mammals on an acute basis.

The risk to small wild mammals from chronic dietary exposure to cyazofamid is expected to be negligible. Exposure of cyazofamid to mice in the diet (6-week) resulted in a NOEL of 7000 mg a.i./kg diet for both lethal and sublethal effects. The EEC of cyazofamid in the mouse diet is much lower, resulting in a RQ of 0.12. Similarly for the rat, the dietary and reproductive risk was negligible as the RQ was 0.04. Therefore, cyazofamid poses a negligible risk to small wild mammals from exposure through their diet.

Offspring development in rats was the most sensitive mammalian endpoint observed (NOAEL = 100 mg a.i./kg bw). A rat would therefore require 0.72 days of continuous feeding on contaminated food sources to reach the NOAEL. Although feeding on contaminated food sources for less than 1 day is considered a potential risk, the number of continuous feeding days to reach the NOEL is nearly a day (0.72 day) for a no-effect level and as such, it is not expected that a substantial risk to offspring development in small mammals will result through feeding on cyazofamid-contaminated food sources. On this basis, the risk of offspring developmental effects in small mammals is expected to be low.

Acute exposure of rats to the transformation products of cyazofamid, CCIM, CCIM-AM, and CTCA was considered. An ultra-conservative scenario of 100% conversion of cyazofamid to each of the transformation products was assumed. On this basis, a rat would require 2.3, 21.5 and 13.2 days of continuous feeding on CCIM, CCIM-AM or CTCA-contaminated food sources, respectively, to reach a dose equivalent to that administered in the laboratory by gavage that killed 50% of the test population. Therefore, the cyazofamid transformation products, CCIM, CCIM-AM and CTCA are expected to pose a negligible risk to small wild mammals on an acute basis.

Terrestrial Plants

Cyazofamid poses a risk to non-target terrestrial plants as demonstrated in vegetative vigour and seedling emergence tests were the RQs were 19.7 and 32.7, respectively, thereby exceeding the LOC (RQ =1).

4.2.1.1. Risk Mitigation

To mitigate the risk (identified above) to beneficial arthropods, small mammals and non-target terrestrial plants, the following precautionary environmental measures are required for the product label (see Appendix X, Label Amendments).

- Beneficial arthropods – precaution on minimizing spray drift to habitats next to the application site
- Small mammals – precaution indicating that the product is toxic to small mammals
- Terrestrial plants – no-spray buffer zone required for use on turf

4.2.2 Risks to Aquatic Organisms

A summary of the risk to aquatic organisms is outlined in Tables 9 and 10 of Appendix I.

To assess the potential for adverse effects, screening level EECs in the aquatic environment were first calculated based on a direct application of 3 x 1060 g a.i./ha at a 14-day interval and an aquatic whole-system representative half-life of 112 days to a 15-cm deep water body representing a seasonal pond suitable for amphibians and an 80-cm deep water body representing a permanent pond. Cyazofamid was assumed to be instantaneously and completely mixed within the water body. The resulting EECs are 1.9 mg a.i./L for a 15 cm deep water body in depth and 0.36 mg a.i./L for a 80 cm deep water body.

At the screening level of assessment, all aquatic organisms were at risk (RQ >1) for the maximum application of cyazofamid to turf (Table 9 in Appendix I). The risk was further characterized (Table 10 in Appendix I) based on more realistic exposure scenarios that are likely to occur under operational field conditions, which include the consideration of spray drift and surface runoff.

Algae and Aquatic Macrophytes

With the refinement in exposure, freshwater algae are at risk from surface runoff (RQ =4.7) and spray drift (RQ = 1.2) entering aquatic habitats. The risk to macrophytes (vascular aquatic plants) is negligible as the RQs are <1 for both spray drift and surface runoff.

Aquatic Invertebrates

The acute and chronic risk to freshwater invertebrates from spray drift and surface runoff is negligible as RQ values are <1.

Fish

The acute and chronic risk to freshwater fish from spray drift and surface runoff is negligible as RQ values are <1.

Amphibians

Amphibians are at risk from exposure to spray drift (RQ = 1.2) and surface runoff (RQ = 2.1) entering aquatic habitats.

Marine algae

Marine algae are at risk from spray drift (RQ = 6.1) and surface runoff (RQ = 24.7).

Marine Invertebrates

Cyazofamid poses a risk to mysid shrimp (RQ = 2.4) through surface runoff. The risk from spray drift is negligible (RQ = 0.60). Similarly, cyazofamid poses a risk to the Eastern oyster through spray drift (RQ = 3.0) and surface runoff (RQ = 12.1).

Marine Fish

Cyazofamid poses a negligible risk to marine fish through spray drift (RQ = 0.21) and surface runoff (RQ = 0.83).

4.2.2.1. Risk Mitigation

To mitigate the risk (identified above) to amphibians, freshwater algae, marine algae and marine invertebrates resulting from surface runoff entering aquatic systems, the proposed product label has the appropriate precautionary measures to mitigate potential risk from this route of exposure.

To mitigate the risk (identified above) to amphibians, freshwater algae, marine algae and marine invertebrates resulting from spray drift entering aquatic systems, no-spray buffer zones are required for the use on turf.

4.2.3 Incident Reports

As of 5 June 2016, no incident reports involving cyazofamid had been submitted to the PMRA.

5.0 Value

5.1 Consideration of Benefits

Cyazofamid provides turf managers with a new fungicide mode of action for the management of turf diseases caused by *Pythium* spp. that can be used in rotation with currently registered products to delay the development of resistance. Please refer to Table 12 for a list of fungicide mode of action groups registered to control or suppress *Pythium* diseases on turf. Multiple alternative fungicides are registered to control or suppress *Pythium* blight and *Pythium* damping-off. A single product is registered to control *Pythium* root dysfunction, belonging to the strobilurin group of fungicides (Group 11). Group 11 fungicides should only be applied once before rotating to a different mode of action when managing *Pythium* diseases in turf. Although this product is registered to be applied up to six times per season, it could only be applied once to manage pythium root dysfunction since there were no alternatives available for rotation. The

ability to alternate with cyazofamid allows superintendents and turf managers to make additional fungicide applications to manage this disease.

Turf disease impacts the playability of golf green by degrading putting surfaces, making courses less attractive to golfers. Maintaining turf quality reduces potential of lost customers and the cost associated with re-establishing turf.

Golf courses in Canada will have access to a fungicide already available to their American counterparts that can improve the performance of current fungicide programs. Registration of this use will allow Canadian golf superintendents to remain competitive with the United States golf industry through equivalent access to technology.

5.2 Effectiveness Against Pests

The applicant submitted 11 efficacy trials and use history information to support the claims. Efficacy trials demonstrated acceptable levels of control of pythium blight and pythium root dysfunction resulting from applications of cyazofamid at the proposed rates and timings. Use history information also provided evidence of acceptable levels of pythium blight, pythium root dysfunction, and pythium damping-off control. The reviewed value information supports the claims as proposed.

5.3 Non-Safety Adverse Effects

No incidents of phytotoxicity from the use of Cyazofamid 400SC Fungicide were reported in the studies submitted. Cyazofamid 400SC Fungicide has been registered in the United States for use on turf with no reported crop tolerance incidents.

5.4 Supported Uses

The reviewed value information was sufficient to support the claims of control of pythium blight, pythium damping-off, and pythium root dysfunction on turf using the indicated use pattern. Details of the supported uses can be found in Table 13 in Appendix 1.

6.0 Pest Control Product Policy Considerations

There were no changes made to the Cyazofamid 400 SC Fungicide formulation since it was last approved by PMRA. On this basis, there are no additional concerns regarding the Toxic Substances Management Policy (TSMP) or with formulants and contaminants that may be of environmental concern.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for cyazofamid is adequate to define the majority of toxic effects that may result from exposure. In short-term and chronic studies on laboratory animals, the majority of studies showed no adverse effects up to the limit dose, other than skin sores and ulceration in male mice, and myocarditis and cataracts in female rats. These findings were

observed following chronic dosing at levels approaching the limit dose. There was no evidence of carcinogenicity in rats or mice after longer-term dosing. There was evidence of increased susceptibility of the young in the rat developmental toxicity study; wavy ribs were observed in fetuses in the absence of maternal toxicity. Cyazofamid was not neurotoxic. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Mixers, loaders and applicators handling Cyazofamid 400 SC Fungicide and workers re-entering treated turf in sod farms and golf courses are not expected to be exposed to levels of cyazofamid that will result in health risks of concern when Cyazofamid 400 SC Fungicide is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

Exposure to the general public re-entering treated golf courses is not expected to result in health risks of concern when Cyazofamid 400 SC Fungicide is used according to label directions.

Please refer to the Regulatory Note REG2006-05 and the Evaluation Report for Sub. No. 2008-1718 for previously reviewed data regarding food residue exposure assessment. The use of cyazofamid on turfgrass in golf courses and sod farms does not constitute a health risk of concern for chronic dietary exposure (food and drinking water) to any segment of the population, including infants, children, adults and seniors.

7.2 Environmental Risk

In soil, biotransformation is the major route of transformation for cyazofamid. Cyazofamid does not undergo photolysis on soil surfaces, but may rapidly phototransform in clear surface waters. Cyazofamid does undergo hydrolysis under environmentally relevant conditions (pH 7), although at a rate slower than that of biotransformation. Cyazofamid is not expected to volatilize under field conditions from soil or surface waters. It is non-persistent in aerobic and anaerobic soils, and is non- to slightly-persistent in aquatic systems. It has the tendency to bind irreversibly to soil and sediment, adsorbs strongly to soils, and is expected to exhibit immobility to low mobility in a variety of soil types. Similarly, it has the tendency to bind irreversibly to aquatic sediment.

The major transformation products found in water were CCIM, CCIM-AM (at pH 9 only), CCTS, HTID, p-toluamide and unidentified polar compounds. In aquatic sediments and soils, the major transformation products were CCIM, CCIM-AM and CTCA. CCIM and CCIM-AM are non-persistent in aerobic soils, while CTCA is persistent with all three expected to exhibit slight to moderate mobility in soils. From field dissipation studies, cyazofamid is not expected to readily leach to groundwater. Due to the long half-life estimates for CTCA in soil (in other words, up to 408 days), it may eventually reach groundwater. Field studies have shown that cyazofamid rapidly dissipates to non-detectable levels and is not expected to carry-over to the following growing season.

In the terrestrial environment, cyazofamid poses a risk to beneficial arthropods and non-target terrestrial plants. A low risk was identified for small mammal offspring development. The risk to other terrestrial organisms from exposure to cyazofamid is negligible.

In the aquatic environment, cyazofamid poses a risk to amphibians, marine invertebrates and freshwater and marine algae through either spray drift of surface runoff entering aquatic systems.

To mitigate the risk (identified above) to beneficial arthropods, small mammals, non-target terrestrial plants, amphibians, freshwater algae, marine algae and marine invertebrates, precautionary environmental measures including no-spray buffer zones are required for the use of cyazofamid on turf.

7.3 Value

Cyazofamid provides turf managers with a new mode of action fungicide for the management of turf diseases caused by *Pythium* spp. that can be used in rotation with currently registered products to delay the development of resistance. Managing diseases minimizes the loss of turf quality, which will reduce economic losses from the costs associated with re-establishing turf. The submitted value information demonstrated acceptable levels of control of pythium blight, pythium damping-off, and pythium root dysfunction from applications of Cyazofamid 400SC Fungicide at the indicated rates and timings.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Technical Cyazofamid Fungicide and Cyazofamid 400 SC Fungicide, containing the technical grade active ingredient cyazofamid, to control diseases caused by the oomycete *Pythium* on turfgrass.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

a.i.	Active Ingredient
ADI	Accepted Daily Intake
ARfD	Acute Reference Dose
ARTF	Agricultural Re-entry Task Force
ATPD	Area Treated per Day
bw	Body Weight
CAF	Composite Assessment Factor
CCIM	4-chloro-5-p-tolylimidazole-2-carbonitrile
CCIM – AM	4-chloro-5-p-tolylimidazole-2-carboxamide
CTCA	4-chloro-5-p-tolylimidazole -2-carboxylic acid
d	Day
DALA	Days After Last Application
DEEM-FCID	Dietary Exposure Evaluation Model - Food Commodity Intake Database
DMSA	Dimethylsulfamic acid
EC_{50}	effective concentration on 50% of the population
ED	Exposure Duration
EEC	Expected Environmental Concentration
EP	End-use product
kg	kilogram
ha	Hectare
LD_{50}	Lethal Dose 50%
LOC	Level of Concern
m^2	Square metre
mg	milligram
ml	millilitre
MOE	Margin of Exposure
MRL	maximum residue limit
NOAEL	No Adverse Effect Level
NOEC	No Observed Effect Concentration
ORETF	Outdoor Residential Exposure Task Force
PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
PHI	Preharvest Interval
PPE	Personal Protective Equipment
ppm	Parts per Million
REI	Restricted Entry Interval
RTI	Retreatment Interval
RQ	Risk Quotient
TC	Transfer Coefficient
TTR	Transferable Turf Residue
USEPA	United States Environmental Protection Agency

Appendix I Tables and Figures

Table 1 Toxicology Endpoints for Use in Health Risk Assessment for Cyazofamid

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary	Not required (No relevant endpoint)		
Repeated dietary	Rat developmental toxicity study	NOAEL = 100 mg/kg bw/day Wavy ribs in fetuses	300
	ADI = 0.33 mg/kg bw/day		
Short- and Intermediate-term dermal[2]	Rat developmental toxicity study	NOAEL = 100 mg/kg bw/day Wavy ribs in fetuses	300
Short- and Intermediate-term inhalation[3]	Rat developmental toxicity study	NOAEL = 100 mg/kg bw/day Wavy ribs in fetuses	300
Cancer	Not required		

[1] CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments

[2] Since an oral NOAEL was selected, a dermal absorption factor of 50% was used in a route-to-route extrapolation as no dermal absorption study was submitted.

[3] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to route extrapolation.

Expected Environmental Concentrations

The expected environmental concentrations (EEC) are used in the risk assessment as an estimate of exposure for identifying the potential risk to aquatic and terrestrial non-target organisms.

Screening Level EECs

As a screening level of exposure, the EECs in habitats of concern are estimated using simple scenarios in which environmental compartments (for example, terrestrial habitats, aquatic habitats or food sources) receive the cumulative application rate of cyazofamid. The EECs are based on the maximum application rates, the number of applications per season, the minimum interval between applications and the transformation of cyazofamid in environmental compartments.

As a broadcast application, potentially there would be exposure to cyazofamid through the deposition of spray drift onto terrestrial habitats, aquatic habitats and food sources. In addition, there is the potential for cyazofamid entering aquatic habitats through surface runoff resulting from broadcast spraying. Table 2 summarizes the maximum EECs in soil and water resulting from the direct overspray of cyazofamid at the maximum single application rate of 1060 g a.i./ha for 3 applications per season with a 14-day application interval and allowing for transformation of cyazofamid between applications.

To account for the transformation of cyazofamid in aquatic systems that occur between applications, an aquatic whole-system representative half-life of 112 days was considered. For transformation in soil between applications, an aerobic soil DT_{50} of 53 days was considered. For transformation on plant surfaces a half-life of 10 days was considered.

Table 2 Maximum EECs: Soil and Water

Use-pattern	Cumulative application rate (g a.i./ha)	EEC in soil (mg a.i./kg soil)[a]	EEC in water (mg a.i./L)	
			15-cm deep pond	80-cm deep pond
Turf	2677.7 (soil)	1.2	-	-
	2923.4 (water)	-	1.9	0.36
	1614.0 (plants)	-	-	-

[a]EEC in soil assumes a soil bulk density of 1.5 g/cm^3, a soil depth of 15 cm.

Refined EECs: Spray Drift

A refined exposure assessment is conducted which considers the off-target spray drift when cyazofamid is applied as a broadcast spray using field sprayers. The off-target spray drift is approximately 6% of the application rate at one meter downwind from the point of application for field sprayers if the spray quality (droplet size distribution) used is classified as ASAE Medium[5]. The 6% value is derived from the PMRA spray drift model for field sprayers based on data generated by Wolf and Caldwell (2001). Table 3 summarizes the refined EECs in soil and water based on spray drift resulting from the broadcast application of cyazofamid at the maximum single application rate of 1060 g a.i./ha for 3 applications per season.

Table 3 Spray Drift EECs: Soil and Water

Use-pattern	Spray drift deposit (g a.i./ha)	EEC in soil (mg a.i./kg soil)[a]	EEC in water (mg a.i./L)	
			15-cm deep pond	80-cm deep pond
Turf	160.7 (soil)	0.07	-	-
	175.4 (water)	-	0.12	0.022
	96.8 (plants)	-	-	-

[a]EEC in soil assumes a soil bulk density of 1.5 g/cm^3, a soil depth of 15 cm.

Refined EECs: Surface Runoff

The following sections review the estimated environmental concentrations (EECs) of cyazofamid resulting from water modelling.

Aquatic Ecoscenario Assessment: Level 1 Modelling

For Level 1 aquatic ecoscenario assessment, estimated environmental concentrations (EECs) of cyazofamid from runoff into a receiving water body were simulated using the SWCC 1.106 model. SWCC runs PRZM5 and VVWM to simulate pesticide runoff from a treated area into an adjacent water body and the fate of a pesticide within that water body. For the Level 1 assessment, the water body consists of a 1 ha wetland with an average depth of 0.8 m and a drainage area of 10 ha.

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5 Droplet size classification system of the American Society of Agricultural Engineers (ASAE) based on the volume median diameter (VMD) of spray droplets.

Modelling was done using a standard turf scenario coupled with seven standard sets of weather data to represent different regions of Canada. Twenty six initial application dates between April and October were modelled. Table 3.5.1.1.1 lists the application information and the main environmental fate characteristics used in the simulations. The EECs are for the portion of the pesticide that enters the water body via runoff only; deposition from spray drift is not included. The models were run for 50 years for all scenarios.

The EECs are calculated from the model output from each run as follows. For each year of the simulation, SWCC calculates peak (or daily maximum) and time-averaged concentrations. The time-averaged concentrations are calculated by averaging the daily concentrations over five time periods (96-hour, 21-day, 60-day, 90-day, and 1 year). The 90th percentiles over each averaging period are reported as the EECs for that period.

The largest EECs of all selected runs of a given use pattern/regional scenario are reported in Tables 4 and 5.

Table 4 Level 1 Aquatic Ecoscenario Modelling EECs (µg a.i./L) for Cyazofamid in a Waterbody 80 cm Deep, Excluding Spray Drift

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Abbotsford	136	89.3	36	15	12.9	2.29
Lethbridge	83.1	53.4	18.1	6.53	4.36	1.08
Winnipeg	102	64.5	20.4	7.59	5.06	1.25
Toronto	78.7	50.3	15.9	5.88	5.32	0.975
Montreal	97.5	63.2	22.3	9.56	6.8	1.4
Charlottetown	87	55	18	6.93	4.83	1.2
NS	132	84	25.7	9.66	6.67	1.6
Maximum	**136**	**89.3**	**36**	**15**	**12.9**	**2.29**

Table 5 Level 1 Aquatic Ecoscenario Modelling EECs (µg a.i./L) for Cyazofamid in a Water Body 15 cm Deep, Excluding Spray Drift

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Abbotsford	720.8	473.29	190.8	79.5	68.37	12.137
Lethbridge	440.43	283.02	95.93	34.609	23.108	5.724
Winnipeg	540.6	341.85	108.12	40.227	26.818	6.625
Toronto	417.11	266.59	84.27	31.164	28.196	5.1675
Montreal	516.75	334.96	118.19	50.668	36.04	7.42
Charlottetown	461.1	291.5	95.4	36.729	25.599	6.36
NS	699.6	445.2	136.21	51.198	35.351	8.48
Maximum	720.8	473.29	190.8	79.5	68.37	12.137

Vegetation and other food sources

As treatments are applied as a broadcast spray, food sources such as insects can be exposed to cyazofamid on-field and thus, would be available to foraging birds and small mammals. Vegetation, however, would only be exposed to cyazofamid off-field through spray drift deposition. Nonetheless, a screening level exposure was considered using the assumption of direct overspray to all food sources as an initial assessment.

For sprayed liquid pesticide formulations, the concentration of pesticide residues on potential food items (vegetation, seeds, insects) is estimated using a nomogram developed by the United States Environmental Protection Agency from the data of Hoerger and Kenaga (1972) and Kenaga (1973), and modified according to Fletcher *et al.*, (1994). Table 6 summarizes the screening level EECs on vegetation and insects resulting from direct application. The EECs were based on the assumption that residues on food sources have a half-life of 10 days. Thus, the cumulative application rate was determined to be 1614 g a.i./ha. It should be noted that for use on turf, short range grass would be the only relevant food item available to herbivores such as geese and rabbits. The estimation of available cyazofamid-contaminated food items is, therefore, a conservative assessment of dietary exposure.

Table 6 Maximum Expected Environmental Concentration (EEC) in Vegetation and Insects After Broadcast Spraying of Cyazofamid

Environmental Compartment	Maximum EEC (mg a.i./kg dry wt.)[a]
short range grass	1139.8
leaves and leafy crops	1988.4
long grass	696.0
forage crops	1045.9
small insects	318.9
pods with seeds	67.4
large insects	54.6
grain and seeds	54.6
fruit	164.4

[a] Estimates from United States Environmental Protection Agency nomogram based on data of Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher *et al.*, (1994).

Table 7 summarizes the EEC in the diet for birds and mammals resulting from the direct broadcast application of cyazofamid. Intake of cyazofamid-contaminated food by foraging birds and mammals is dependent on the amount and type of food consumed. The bobwhite diet may consist of approximately 30% small insects, 15% forage crops, and 55% grain and seeds. The EEC in the bobwhite diet after the application of cyazofamid, based on the cumulative application rate on food sources (1614 g a.i./ha) is 282.6 mg a.i./kg dw diet (Table 7). The mallard diet consists of approximately 30% large insects and 70% grain and seeds. The EEC in the mallard diet is 54.6 mg a.i./kg dw diet.

Table 7 Estimated Maximum Daily Exposure (EDE) for Birds and Mammals

Food	EEC	% of diet	EEC each food	READ E EEC in diet	
Bobwhite quail					
small insects	318.926	30	95.68		
forage crops	1045.876	15	156.88		
grain	54.585	55	30.02	**282.58**	mg a.i./kg dw
Mallard duck					
arthropods [1]	54.585	30	16.38		
grain	54.585	70	38.21	**54.59**	mg a.i./a.i./kg dw
Rat					
short grass	1139.831	70	797.88		
grain/seeds	54.585	20	10.92		
large insects	54.585	10	5.46	**814.26**	mg a.i./kg dw
Mouse					
short grass	1139.831	25	284.96		
grain/seeds	54.585	50	27.29		
leaves/leafy crops	1988.442	25	497.11	**809.36**	mg a.i./kg dw
Rabbit					
short grass	1139.831	25	284.96		
leaves/leafy crops	1988.442	25	497.11		
long grass	695.956	25	173.99		
forage crops	1045.876	25	261.47	**1217.53**	mg a.i./kg dw

Table 8 Risk to Terrestrial Organisms

Organism	Exposure		Endpoint value	EEC	RQ	Risk
Invertebrates						
Earthworm	Acute		NOEC = 1000 mg a.i./kg	1.2 mg a.i./kg	0.0012	Negligible
Bee	Oral		NOEC = 100 µg a.i./bee (112000 g a.i./ha)	3180 g a.i./ha	0.03	Negligible
	Contact		NOEC = 150 µg a.i./bee (170200 g a.i./ha)	3180 g a.i./ha	0.02	Negligible
Parasitic arthropod	Contact		NOEC = 200 g a.i./ha	3180 g a.i./ha	16.0	Risk to beneficial arthropods
Birds						
Bobwhite quail	Acute		NOEL = 2000 mg a.i./kg bw	282.6 mg a.i./kg diet	82.6 days of feeding exclusive feeding on contaminated food to reach the NOEL	Negligible
	Dietary		NOEL = 4989 mg a.i./kg diet	282.6 mg a.i./kg diet	0.06	Negligible
	Reproduction		NOEL = 5030 mg a.i./kg diet	282.6 mg a.i./kg diet	0.06	Negligible
Mallard duck	Dietary		NOEL = 4740 mg a.i./kg diet	54.6 mg a.i./kg diet	0.011	Negligible
	Reproduction		NOEL = 5100 mg a.i./kg diet	54.6 mg a.i./kg diet	0.010	Negligible
Mammals						
Rat	Acute	Cyazofamid	LD_{50} > 5000 mg a.i./kg bw	814.3 mg a.i./kg diet	35.8 days of exclusive feeding on contaminated food to reach the LD_{50}	Negligible
		CCIM	LD_{50} = 324 mg/kg bw	814.3 mg/kg diet (based on 100% conversion of parent; therefore extremely conservative)	2.3 days of exclusive feeding on contaminated food to reach the LD_{50}	Negligible
		CCIM-AM	LD_{50} > 3000 mg/kg bw	814.3 mg/kg diet (based on 100% conversion of	21.5 days of exclusive feeding on	Negligible

Organism	Exposure		Endpoint value	EEC	RQ	Risk
				parent; therefore extremely conservative)	contaminated food to reach the LD_{50}	
		CTCA	LD_{50} = 1839 mg/kg bw	814.3 mg/kg diet (based on 100% conversion of parent; therefore extremely conservative)	13.2 days of exclusive feeding on contaminated food to reach the LD_{50}	Negligible
	Dietary (4-week)		NOAEL = 20000 mg a.i./kg diet	814.3 mg a.i./kg diet	0.04	Negligible
	Reproduction (multi-generation dietary)		Parental, Offspring, and Reproductive: NOAEL = 20000 mg a.i./kg diet	814.3 mg a.i./kg diet	0.04	Negligible
	Developmental (gavage study)		NOAEL: 100 mg/kg bw/d	814.3 mg a.i./kg diet	0.72 days of exclusive feeding on contaminated food to reach the NOAEL	Low
Mouse	Acute		LD_{50} > 5000 mg a.i./kg bw	809.4 mg a.i./kg diet	34 days of exclusive feeding on contaminated food to reach the LD_{50}	Negligible
	Dietary (6-week)		NOAEL = 7000 mg a.i./kg diet	809.4 mg a.i./kg diet	0.12	Negligible
Rabbit	Developmental (gavage study)		NOAEL = 1000 mg/kg bw/d	1217.5 mg a.i./kg diet	27.4 days days of exclusive feeding on contaminated food to reach the NOAEL	Negligible
Vascular plants						
Vascular plant	Seedling emergence and vegetative vigour		EC_{25} > 82 g a.i./ha	2677.7 g a.i./ha (soil) 1614 g a.i./ha (foliage)	32.7 (seedling emergence) 19.7 (vegetative vigour)	Risk

Table 9 Screening Level Risk to Aquatic Organisms

Organism	Exposure	End point value	EEC	RQ	Risk
Freshwater species					
Daphnia magna	Acute	NOEC = 0.107 mg a.i./l	0.36 mg a.i./L	3.4	Risk
	Chronic	NOEC = 0.107 mg a.i./l	0.36 mg a.i./L	3.4	Risk
Chironomus riparius	Acute	NOEC =0.095 mg a.i./l	0.36 mg a.i./L	3.8	Risk
Rainbow trout	Acute	NOEC = 0.107 mg a.i./l	0.36 mg a.i./L	3.4	Risk
Bluegill sunfish	Acute	NOEC = 0.107 mg a.i./l	0.36 mg a.i./L	3.4	Risk
Fathead minnow	Chronic	NOEC = 0.0901 mg a.i./l	0.36 mg a.i./L	4.0	Risk
Amphibian	Chronic	NOEC = 0.0901 mg a.i./l	1.9 mg a.i./L	21.1	Risk
Freshwater algae (diatoms)	Acute	NOEC = 0.019 mg a.i./L	0.36 mg a.i./L	18.9	Risk
Vascular plant	Dissolved	NOEC = 0.107 mg a.i./l	0.36 mg a.i./L	3.4	Risk
Marine species					
Crustaccan (mysid shrimp)	Acute	NOEC = 0.0369 mg a.i./l	0.36 mg a.i./L	9.8	Risk
Mollusk (Eastern oyster)	Acute	½ EC_{50} = 0.00735	0.36 mg a.i./L	49.0	Risk
Sheepshead minnow	Acute	NOEC = 0.107 mg a.i./l	0.36 mg a.i./L	3.4	Risk
Marine algae (diatom)	Acute	NOEC = 0.0036 mg a.i./l	0.36 mg a.i./L	100	Risk

Table 10 Summary of Tier I Refined Aquatic Risk Assessment

Organism	Exposure	Endpoint value (mg a.i./L)	EEC spray drift (mg a.i./L)	EEC Runoff (mg a.i./L)	RQ Spray drift	RQ - runoff
Freshwater species						
Daphnia magna	Acute	NOEC = 0.107	0.022	0.089[A]	0.21	0.83
	Chronic	NOEC = 0.107	0.022	0.036[B]	0.21	0.34
Chironomus riparius	Acute	NOEC =0.095 mg a.i./l	0.022	0.089	0.23	0.93
Rainbow trout	Acute	NOEC = 0.107	0.022	0.089[A]	0.21	0.83
Bluegill sunfish	Acute	NOEC = 0.107	0.022	0.089[A]	0.21	0.83
Fathead minnow	Chronic	NOEC = 0.0901	0.022	0.036[B]	0.24	0.40
Amphibian	Chronic	NOEC = 0.0901	0.11	0.19[C]	1.2	2.1
Freshwater algae (diatoms)	Acute	NOEC = 0.019	0.022	0.089[A]	1.2	4.7
Vascular aquatic plant	Dissolved	NOEC = 0.107	0.022	0.089[A]	0.21	0.83
Marine species						
Crustacean (mysid shrimp)	Acute	NOEC = 0.0369	0.022	0.089[A]	0.60	2.4
Mollusk (Eastern oyster)	Acute	½ EC_{50} = 0.00735	0.022	0.089[A]	3.0	12.1
Sheepshead minnow	Acute	NOEC = 0.107	0.022	0.089[A]	0.21	0.83
Marine algae (diatom)	Acute	NOEC = 0.0036	0.022	0.089[A]	6.1	24.7

[A]96-hour EEC. [B]21-day EEC. [C]21-day EEC for amphibian habitat.

Table 11 Food Residue Chemistry Overview of Risk Assessment

DIETARY RISK FROM FOOD AND DRINKING WATER		
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**
		Food and Drinking Water
Basic chronic non-cancer dietary risk **ADI = 100 mg/kg bw/day** **Estimated chronic drinking water concentration = 22 Φg a.i./L**	**All infants <1 year**	1.9
	Children 1-2 years	4.9
	Children 3-5 years	4.1
	Children 6-12 years	2.4
	Youth 13-19 years	1.7
	Adults 20-49 years	2.2
	Adults 50+ years	2.1
	Females 13-49 years	2.2
	Total population	2.3

Table 12 Registered Alternatives Based on Mode of Action (as of July 2015)

Disease	Mode of Action Group No.
pythium blight	11, 33, U
pythium damping-off	4, U
pythium root dysfunction	11

Table 13 List of Supported Uses

Diseases	Supported use pattern
pythium blight (*Pythium aphanidermatum*) pythium damping-off (*Pythium* spp.) pythium root dysfunction (*Pythium volutum*)	**Rates:** 14.3 – 26.6 ml/100 m^2 (5.7 – 10.6 g a.i./100 m^2) **Spray interval:** 14 – 21 days **Spray volume:** 7.5 – 15.0 L of water/100m^2 **Maximum seasonal applications/rate:** Apply up to three times per season with a maximum seasonal application rate of 80 ml/100 m^2 (32 g a.i./100 m^2) **Other:** After one application, alternate **Cyazofamid 400SC Fungicide** with at least one application of fungicide having a different mode of action. Use the lower rate for the shortest interval and higher rate for the longest interval. The high rate and short interval should be used when disease pressure is severe.

References

A. List of Studies/Information Submitted by Registrant

1.0 Human and Animal Health

PMRA #	References
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2.0 Value

2506212 2015, Value Summary for Cyazofamid 400SC Fungicide Label Expansion for Control of Pythium Blight, Pythium Root Dysfunction and Pythium Damping Off in Turf, DACO: 10.1,10.2,10.2.1,10.2.2,10.2.3,10.2.3.1,10.2.3.2,10.2.3.3,10.3,10.3.1,10.3.2,10.3.3,10.4,10.5,10.5.2,10.5.3